

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 27 February 2001 (27.02.01)
International application No. PCT/US00/18348
International filing date (day/month/year) 05 July 2000 (05.07.00)
Applicant BRIDGES, Alexander, James et al

Applicant's or agent's file reference
A0000100-01E

Priority date (day/month/year)
16 July 1999 (16.07.99)

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:
18 January 2001 (18.01.01)

in a notice effecting later election filed with the International Bureau on:

2. The election was
 was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Zakaria EL KHODARY Telephone No.: (41-22) 338.83.38
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Facsimile No.: (41-22) 740.14.35

Form PCT/IB/331 (July 1992)

US0018348

PATENT COOPERATION TREATY
NOTED

From the INTERNATIONAL SEARCHING AUTHORITY

JAN 26 2001

(Handwritten mark)
PCT

To:	K. STRITENBERGER
WARNER-LAMBERT COMPANY Attn. RYAN, M. Andrea 201 Tabor Road Morris Plains, New Jersey 07950 UNITED STATES OF AMERICA	NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing (day/month/year)	23/01/2001
Applicant's or agent's file reference A0000100-01E	FOR FURTHER ACTION	See paragraphs 1 and 4 below
International application No. PCT/US 00/ 18348	International filing date (day/month/year)	05/07/2000

Applicant

WARNER-LAMBERT COMPANY et al.

1. The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Joannes Vergoosen

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/ is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (c) (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference A0000100-01E	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 18348	International filing date (day/month/year) 05/07/2000	(Earliest) Priority Date (day/month/year) 16/07/1999
Applicant WARNER-LAMBERT COMPANY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
- 2. Certain claims were found unsearchable (See Box I).
- 3. Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 00/18348

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The invention features a method for treating chronic pain using a compound selected from formulae I, II A, I B, I C as shown in the claims.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/18348

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	A61K31/18	A61K31/185	A61K31/63	A61K31/196	A61K31/166
	A61K31/4164	A61K31/433	A61P25/04		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 42002 A (WARNER LAMBERT CO ;TECLE HAILE (US)) 20 July 2000 (2000-07-20) cited in the application examples 7,8 claims 1-18,29 ---	1,4,7,8, 10-26, 122
E	WO 00 42003 A (BARRETT STEPHEN DOUGLAS ;WARNER LAMBERT CO (US); TECLE HAILE (US);) 20 July 2000 (2000-07-20) cited in the application claims 1-20,29,30; examples 14,15 ---	95,98, 102, 104-121, 125
E	WO 00 41994 A (BARRETT STEPHEN DOUGLAS ;WARNER LAMBERT CO (US); TECLE HAILE (US)) 20 July 2000 (2000-07-20) cited in the application claims 1-25,34,35; examples 8,9 ---	27,30, 34, 36-58, 123
-/--		

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

12 January 2001

23/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Veronese, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/18348

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 41505 A (BARRETT STEPHEN DOUGLAS ;WARNER LAMBERT CO (US); TECLE HAILE (US)) 20 July 2000 (2000-07-20) cited in the application claims 1-28,38,39 ---	59,62, 66,68-94
X	EP 0 316 630 A (WARNER LAMBERT CO) 24 May 1989 (1989-05-24) page 8, line 3-8; claims 1-44,9,14,15,17; examples 13,18 page 8, line 40,41 ---	59,62, 65,66, 69,71
X	FUJIMURA H ET AL: "HYDROXAMIC ACID DERIVATIVES" CHEMICAL ABSTRACTS + INDEXES, AMERICAN CHEMICAL SOCIETY. COLUMBUS, US, vol. 70, no. 3, 20 January 1969 (1969-01-20), XP002142605 ISSN: 0009-2258 abstract & JP 42 024578 A (TAKEDA CHEMICAL INDUSTRIAL LTD) 1967 ---	59,62, 65,70
X	MOKHORT N A: "DEPENDENCE BETWEEN STRUCTURE, ANTIINFLAMMATORY, ANALGESIC, AND ANTIPYR" CHEMABS, AN =1972:121461, 1972, XP002142610 abstract ---	59,62, 65,69
X	HIRANO HIROSHI ET AL: "NOVEL N-PHENYLANTHRANILIC ACID DERIVATIVES" CHEMABS, AN = 1968:418858, 1968, XP002142611 abstract ---	59,62, 65,69,77
Y	WO 99 01421 A (DOHERTY ANNIE MARIAN ;BARRETT STEPHEN DOUGLAS (US); BRIDGES ALEX) 14 January 1999 (1999-01-14) claim 1; example 212 ---	1-125
P,Y	JI RU-RONG ET AL: "Nociceptive-specific activation of ERK in spinal neurons contributes to pain hypersensitivity." NATURE NEUROSCIENCE, vol. 2, no. 12, December 1999 (1999-12), pages 1114-1119, XP000978586 ISSN: 1097-6256 page 1117, column 2; figure F ---	1-125
A	WO 98 37881 A (BRIDGES ALEXANDER JAMES ;WARNER LAMBERT CO (US)) 3 September 1998 (1998-09-03) the whole document ---	1-125
1	-/-	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/18348

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DUESBERY N S ET AL: "MEK WARS, A NEW FRONT IN THE BATTLE AGAINST CANCER" NATURE MEDICINE, US, NATURE PUBLISHING, CO, vol. 5, no. 7, 1999, pages 736-737, XP000907246 ISSN: 1078-8956 the whole document ---	1-125
A	DUNCIA J V ET AL: "MEK inhibitors: the chemistry and biological activity of U0126, its analogs, and cyclization products" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, GB, OXFORD, vol. 8, no. 20, 20 October 1998 (1998-10-20), pages 2839-2844, XP004139571 ISSN: 0960-894X the whole document ---	1-125
A	US 2 502 451 A (A A GOLDBERG) 4 April 1950 (1950-04-04) the whole document -----	59-94

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/18348

B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-125 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/18348

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0042002	A	20-07-2000	AU 2482800 A		01-08-2000
			JP 2000204075 A		25-07-2000
WO 0042003	A	20-07-2000	AU 2201500 A		01-08-2000
			JP 2000212157 A		02-08-2000
WO 0041994	A	20-07-2000	AU 2482900 A		01-08-2000
			JP 2000204068 A		25-07-2000
WO 0041505	A	20-07-2000	AU 2483400 A		01-08-2000
			JP 2000212141 A		02-08-2000
EP 0316630	A	24-05-1989	US 5155110 A		13-10-1992
			AU 2909289 A		23-05-1989
			WO 8903818 A		05-05-1989
			ZA 8807696 A		27-06-1990
WO 9901421	A	14-01-1999	AU 8262698 A		25-01-1999
			BR 9810385 A		05-09-2000
			EP 0993437 A		19-04-2000
			HR 980369 A		30-04-1999
			ZA 9805726 A		27-01-1999
WO 9837881	A	03-09-1998	AU 5610398 A		18-09-1998
			ZA 9801578 A		02-09-1998
US 2502451	A	04-04-1950	FR 930361 A		28-01-1948
			GB 608492 A		
			NL 62219 C		

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A0000100-01E	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/18348	International filing date (day/month/year) 05/07/2000	Priority date (day/month/year) 16/07/1999
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant WARNER-LAMBERT COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 18/01/2001	Date of completion of this report 18.06.2001
Name and mailing address of the International preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Cattell, James Telephone No. +49 89 2399 8468



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/18348

I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-116 as originally filed

Claims, No.:

1-127 as originally filed

Drawings, sheets:

1/8-8/8 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/18348

the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c));

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-58, 60-68, 71-73, 75, 76, 78-80, 84, 86-127
No: Claims 59, 69, 70, 74, 77, 81, 82, 83, 85

Inventive step (IS) Yes: Claims 1-58, 60-68, 71-73, 75, 76, 78-80, 84, 86-127
No: Claims

Industrial applicability (IA) Yes: Claims 1-127
No: Claims

**2. Citations and explanations
see separate sheet**

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/18348

V.

- 1). Document D1 (EP-A-0 316 630) discloses in Formula I compounds similar to those of the present claims 59 and 95. It is however clear from the examples of D1 that the present claims represent a selection from D1 as the "J" group or "I" can only be at position 4. D1 page 8 line 8 discloses the compounds for the treatment of pain.

Document D2 (FUJIMURA et al 1969) discloses a 4-methylphenyl derivative as an analgesic. This compounds falls within the scope of claims 59, 70, 74, 81, 82, 83 and 85 under Article 33(2) PCT.

Document D3 (MOKHORT N A: 'DEPENDENCE BETWEEN STRUCTURE, ANTIINFLAMMATORY, ANALGESIC, AND ANTIPYR' CHEMABS, AN =1972:121461, 1972) discloses 2-[(4-methylphenyl)amino]-benzoic acid as an analgesic. This disclosure falls within the scope of claims 59, 69, 74, 81 and 82 under Article 33(2) PCT.

Document D4 (HIRANO HIROSHI ET AL: 'NOVEL N-PHENYLANTHRANILIC ACID DERIVATIVES' CHEMABS, AN = 1968:418858, 1968) discloses 2-[(4-methyl sulphonyl phenyl)amino]-benzoic acid as an analgesic, falling within the scope of claims 59, 69, 74, 77, 81 and 82 under Article 33(2) PCT.

- 2). Document D5 and D6 (WO 99 01421 and WO 98 37881) discloses similar compounds as MEK inhibitors, but not for the treatment of pain.
- 3). None of D1 to D4 suggest that MEK inhibitors could be used to treat pain. The section of novel compounds from D1 or an alteration of the structure of compounds from D2 to D4 would not therefore be obvious to the skilled man.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/18348

VIII.

- 4). For the assessment of the present claims 1-127 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.